Fentanyl rotation from subcutaneous to transdermal administration: A validation of current practice

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To prospectively validate the pharmacokinetics of fentanyl during the current standard-of-care rotation scheme from subcutaneous to transdermal fentanyl administration in patients with moderate to severe cancer-related pain. We aim to prove bio-...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON54225

Source
ToetsingOnline

Brief title
FARAO

Condition

- Other condition

Synonym
Cancer pain, Cancer-related pain

Health condition

Kanker gerelateerde pijn

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cancer, Fentanyl, Pain, Rotation

Outcome measures

Primary outcome

To prove bioequivalence in fentanyl exposure (measured as area under the curve

(AUC)) pre- and post-rotation.

Secondary outcome

To associate the occurrence and severity of adverse events and pain scores pre-

and post-rotation with pharmacokinetic parameters.

Study description

Background summary

Fentanyl is a strong-acting, widely used opioid in the treatment of cancer-related pain. In hospitalized patients with severe pain, fast dose titration of fentanyl can be performed by combined continuous and bolus subcutaneous administration. When stable pain control is reached, a rotation to transdermal patches can be done. The fentanyl rotation-scheme used in Erasmus MC was previously based on data concerning rotation from intravenous fentanyl. Based on a PK modeling study with subcutaneous fentanyl (METC nr.09-332) and clinical observations, the fentanyl rotation scheme has been optimized and the rotation scheme is now used in standard clinical practice. However, this scheme has never been validated prospectively on PK and PD-endpoints.

Study objective

To prospectively validate the pharmacokinetics of fentanyl during the current standard-of-care rotation scheme from subcutaneous to transdermal fentanyl administration in patients with moderate to severe cancer-related pain. We aim to prove bio-equivalence before and after fentanyl rotation using the area

under the curve (AUC).

Study design

Real-life observational study in patients who are rotated from a subcutaneous to a transdermal administration route for fentanyl according to the current standard of care in the Erasmus Medical Centre. Due to the use of the previously developed model the number of blood samples will be very sparse. We plan to collect 2-3 randomly taken samples prior to the rotation and 2-3 random samples after the rotation. The acquired exposure quantified as AUC will be compared pre- and post-rotation with a paired t-test. Patients complete the study when all blood samples are taken or when the patient is discharged from the hospital.

Study burden and risks

The risk of the extra blood withdrawals is negligible.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Age >=18 years;
- Able to understand the written information and able to give informed consent.
- Current treatment with subcutaneous fentanyl and planned to rotate to transdermal fentanyl
- To ensure steady-state kinetics, patients must have been treated with subcutaneous fentanyl for at least 40 hours prior to the rotation and have been treated with a stable fentanyl dose at least 20 hours prior to the rotation
This way, fentanyl pharmacokinetics are at steady-state.

Exclusion criteria

- Patients that use short-acting fentanyl via the oral, (oral mucosal, sublingual), intranasal or subcutaneous administration route 12 hours prior to the rotation will be excluded as this influences the pharmacokinetic profile of the subcutaneous administration. This implicates that patients will be prescribed oral short acting oxycodone or morphine 12 hours before rotation as these are mostly used next to treatment with transdermal fentanyl.
- Patients that use strong CYP3A4 inhibitors or inducers, as spacified by the KNMP kennisbank, will be excluded as the model did not account for the influence of strong CYP3A4 inhibition or induction on fentanyl pharmacokinetics while the effects have been shown in multiple studies.
- Patients that are rotated using a dose conversion ratio other than 1:1 will also be excluded.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-12-2022
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	04-11-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-03-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL78595.078.21